(2) a second probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set that includes the at least one interrogation position, except that the at least one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein, the probes in the first probe set have at least three interrogation positions respectively corresponding to each of at least three contiguous nucleotides in the reference sequence, and

(b) detecting a hybridization pattern of the oligonucleotide probes to the target nucleic acid and determining from the hybridization pattern whether a nucleotide in the target sequence is the same or different from the corresponding nucleotide in the reference sequence.

Please amend claim 88 as follows:

88. (Amended) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

(a) hybridizing the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:

a perfectly matched probe exactly complementary to a subsequence of a reference sequence, the perfectly matched probe having a plurality of interrogation positions respectively corresponding to a plurality of nucleotides in the reference sequence,

for each interrogation position, three mismatched probes, each identical to the perfectly matched probe including the plurality of interrogation positions, except in the interrogation position, which is occupied by a different nucleotide in each of the three mismatched probes and the perfectly matched probe;

(b) for each interrogation position,

(1) comparing the relative specific binding of the three mismatched probes and the perfectly matched probe;

(2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greatest specific binding.

Please amend claim 90 as follows:

90. (Amended) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

hybridizing the target sequence to an array of oligonucleotide probes immobilized on a solid support, the array comprising at least one pair of first and second probe groups, each group comprising a first and second sets of oligonucleotide probes,

the first probe set comprising a plurality of probes, each probe exactly complementary to a subsequence of a reference sequence, the segment including at least one interrogation position complementary to a corresponding nucleotide in the reference sequence,

the second probe set comprising a corresponding probe for each probe in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set, except that the at least one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein the probes in the first probe set have at least three interrogation positions respectively corresponding to each of three contiguous nucleotides in the reference sequence;

wherein each probe in the first probe set from the first group is exactly complementary to a subsequence of a first reference sequence and each probe in the first probe set from the second group is exactly complementary to a subsequence from a second reference sequence;

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determining which probes in the first group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the first reference sequence;

determining which probes in the second group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the second reference sequence.

REMARKS

Applicants respond to the Examiner's comment using the paragraph numbering of the office action.

7. Handwritten notations are not intended to be part of the specification. SEQ ID NOS. are inserted by the amendment indicated above.

8-9. The claims stand rejected for lack of enablement on the basis that the length of probes and reference sequence is critical to the practice of the invention but not included in the claims. The Examiner says that probes must be sufficiently long to hybridize to the reference sequence. The Examiner also makes various comments regarding the reference sequence. This rejection is respectfully traversed.

With respect to probe length, it is already inherent in the claims that an array should include probes of sufficient length to hybridize to the target sequence, because otherwise there would be no hybridization pattern as recited in step (b) of the claim. Thus, the issue in determining enablement is whether undue experimentation would be required for the a skilled person to know which probes were of suitable length. The specification indicates that that probe typically include 6-30 complementary